



## RNAse T2-deficient leukoencephalopathy

RNAse T2-deficient leukoencephalopathy is a disorder that affects the brain. People with RNAse T2-deficient leukoencephalopathy have neurological problems that become apparent during infancy; the problems generally do not worsen over time (progress). Most affected individuals have severe intellectual disability; muscle stiffness (spasticity); and a delay in developing motor skills such as sitting, crawling, and walking. Some do not learn to walk, and most do not develop the ability to speak. Other neurological features that can occur in RNAse T2-deficient leukoencephalopathy include hearing loss caused by abnormalities in the inner ear (sensorineural deafness), seizures, involuntary writhing movements of the hands (athetosis), uncontrolled muscle tensing (dystonia), and involuntary eye movements (nystagmus). In addition to the neurological problems associated with this disorder, some affected individuals have unusual facial features sometimes described as a "doll-like face."

The neurological problems in this disorder are caused by abnormalities in the brain. People with this condition have leukoencephalopathy, an abnormality of the brain's white matter that can be detected with medical imaging. White matter consists of nerve fibers covered by a fatty substance called myelin. Myelin insulates nerve fibers and promotes the rapid transmission of nerve impulses. In people with RNAse T2-deficient leukoencephalopathy, myelin is not made in sufficient amounts during development, leading to patchy white matter abnormalities (lesions) in the brain. In addition, individuals with RNAse T2-deficient leukoencephalopathy may have cysts in regions of the brain called the temporal lobes and enlargement of the fluid-filled cavities (ventricles) near the center of the brain. The white matter lesions are primarily concentrated around the cysts and the ventricles. An abnormally small head and brain size (microcephaly) often occurs in this disorder.

### Frequency

The prevalence of RNAse T2-deficient leukoencephalopathy is unknown. About 50 people with the signs and symptoms of this disorder have been described in the medical literature. However, only about a quarter of these individuals have been confirmed to have the same genetic change that causes RNAse T2-deficient leukoencephalopathy. Researchers suggest that additional genetic changes or other causes may also result in the same pattern of signs and symptoms (phenotype).

### Genetic Changes

RNAse T2-deficient leukoencephalopathy is caused by mutations in the *RNASET2* gene. This gene provides instructions for making a protein called ribonuclease T2

(RNAse T2), which is normally abundant in the brain. Ribonucleases help break down RNA, a chemical cousin of DNA. Studies suggest that ribonuclease T2 may also be involved in other functions within cells, such as controlling the development of blood vessels (angiogenesis) and helping to suppress the growth of cancerous tumors. These potential roles of the protein are not well understood.

The *RNASET2* gene mutations that cause RNAse T2-deficient leukoencephalopathy result in loss of ribonuclease T2 protein function. It is unknown how loss of this protein results in brain abnormalities and neurological problems. Researchers have noted that the signs and symptoms of RNAse T2-deficient leukoencephalopathy are similar to those resulting from infection with a particular virus, called cytomegalovirus (CMV), when it is transmitted to a fetus during pregnancy (congenital CMV). They are seeking to understand how the viral infection, or the body's response to it, and the loss of ribonuclease T2 function could have similar effects on the developing brain. It is thought that both may be related to changes in angiogenesis or an immune system response to RNA that has not been properly broken down.

## **Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## **Other Names for This Condition**

- cystic leukoencephalopathy without megalencephaly
- LBATC
- leukoencephalopathy with bilateral anterior temporal lobe cysts
- RNASET2-deficient cystic leukoencephalopathy

## **Diagnosis & Management**

### Genetic Testing

- Genetic Testing Registry: Leukoencephalopathy, cystic, without megalencephaly  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2751843/>

### Other Diagnosis and Management Resources

- GeneReview: Leukodystrophy Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK184570>
- MedlinePlus Encyclopedia: Head MRI  
<https://medlineplus.gov/ency/article/003791.htm>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

### **Additional Information & Resources**

#### MedlinePlus

- Encyclopedia: Head MRI  
<https://medlineplus.gov/ency/article/003791.htm>
- Health Topic: Leukodystrophies  
<https://medlineplus.gov/leukodystrophies.html>

#### Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Leukodystrophy Information Page  
<https://www.ninds.nih.gov/Disorders/All-Disorders/Leukodystrophy-Information-Page>

#### Educational Resources

- Children's Hospital of Philadelphia: Leukodystrophy  
[http://www.chop.edu/conditions-diseases/leukodystrophy#.V7Ms4\\_krIQh](http://www.chop.edu/conditions-diseases/leukodystrophy#.V7Ms4_krIQh)
- Cleveland Clinic: Leukodystrophy  
<http://my.clevelandclinic.org/health/articles/leukodystrophy>
- Kennedy Krieger Institute: Leukodystrophy  
<https://www.kennedykrieger.org/patient-care/diagnoses-disorders/leukodystrophy>
- Orphanet: Cystic leukoencephalopathy without megalencephaly  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=85136](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=85136)
- VU University Medical Center (Amsterdam): White Matter Disorders  
<https://www.vumc.com/branch/Children-White-Matter-Disorders/419542/>

### Patient Support and Advocacy Resources

- Mission Massimo Foundation  
<http://www.missionmassimo.com/leukodystrophy/>
- National Organization for Rare Disorders: Leukodystrophy  
<https://rarediseases.org/rare-diseases/leukodystrophy/>
- The Brain Foundation (Australia)  
<http://brainfoundation.org.au/>
- United Leukodystrophy Foundation  
<http://ulf.org/>

### GeneReviews

- Leukodystrophy Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK184570>

### ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22RNase+T2-deficient+leukoencephalopathy%22+OR+%22Hereditary+Central+Nervous+System+Demyelinating+Diseases%22+OR+%22cystic+leukoencephalopathy+without+megalencephaly%22>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28RNase+T2-deficient+leukoencephalopathy%29+OR+%28cystic+leukoencephalopathy+without+megalencephaly%29+OR+%28RNASET2-deficient+cystic+leukoencephalopathy%29+OR+%28leukoencephalopathy+with+bilateral+anterior+temporal+lobe+cysts%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

### OMIM

- LEUKOENCEPHALOPATHY, CYSTIC, WITHOUT MEGALENCEPHALY  
<http://omim.org/entry/612951>

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